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**MyoD targets TAF3/TRF3 to activate myogenin transcription.**

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**Public Summary:**

**Scientific Abstract:**

Skeletal muscle differentiation requires a cascade of transcriptional events to control the spatial and temporal expression of muscle-specific genes. Until recently, muscle-specific transcription was primarily attributed to prototypic enhancer-binding factors, while the role of core promoter recognition complexes in directing myogenesis remained unknown. Here, we report the development of a purified reconstituted system to analyze the properties of a TAF3/TRF3 complex in directing transcription initiation at the Myogenin promoter. Importantly, this new complex is required to replace the canonical TFIID to recapitulate MyoD-dependent activation of Myogenin. In vitro and cell-based assays identify a domain of TAF3 that mediates coactivator functions targeted by MyoD. Our findings also suggest changes to CRSP/Mediator in terminally differentiated myotubes. This switching of the core promoter recognition complex during myogenesis allows a more balanced division of labor between activators and TAF coactivators, thus providing another strategy to accommodate cell-specific regulation during metazoan development.

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